

Real-World Use of Trofinetide: A Survey of Tolerability From US Rett Syndrome Centers of Excellence

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BACKGROUND

- Rett syndrome (RTT) is a rare neurodevelopmental disorder characterized by loss of verbal communication with limited nonverbal skills, loss of fine and gross motor function, behavioral issues, seizures, hand stereotypies, and gastrointestinal problems^{1,2}
- Trofinetide was approved by the US Food and Drug Administration in March 2023 for the treatment of RTT in adults and pediatric patients aged ≥2 years³
- Diarrhea was the most common adverse event and the leading cause of treatment discontinuation in clinical trials⁴⁻⁶; dose titration strategies are being used to improve tolerability in the real world

OBJECTIVE

- To explore real-world experience with trofinetide dose titration and its impact on tolerability in the real world

METHODS

Study Design

- An electronic prescriber experience survey was designed to collect real-world trofinetide dosing strategies and their impact on tolerability
- The survey was sent in May 2024 to 33 prescribers at 18 US RTT centers of excellence (COEs) designated by the International Rett Syndrome Foundation

Data Analysis

- All results were summarized with descriptive statistics

RESULTS

Study Participation

- Overall, 22 prescribers from 16 COEs completed the electronic survey
- The prescribers targeted for survey completion accounted for 38.1% of trofinetide prescriptions in the United States since approval (**Table 1**)

Table 1. Electronic Survey Participation and Representation

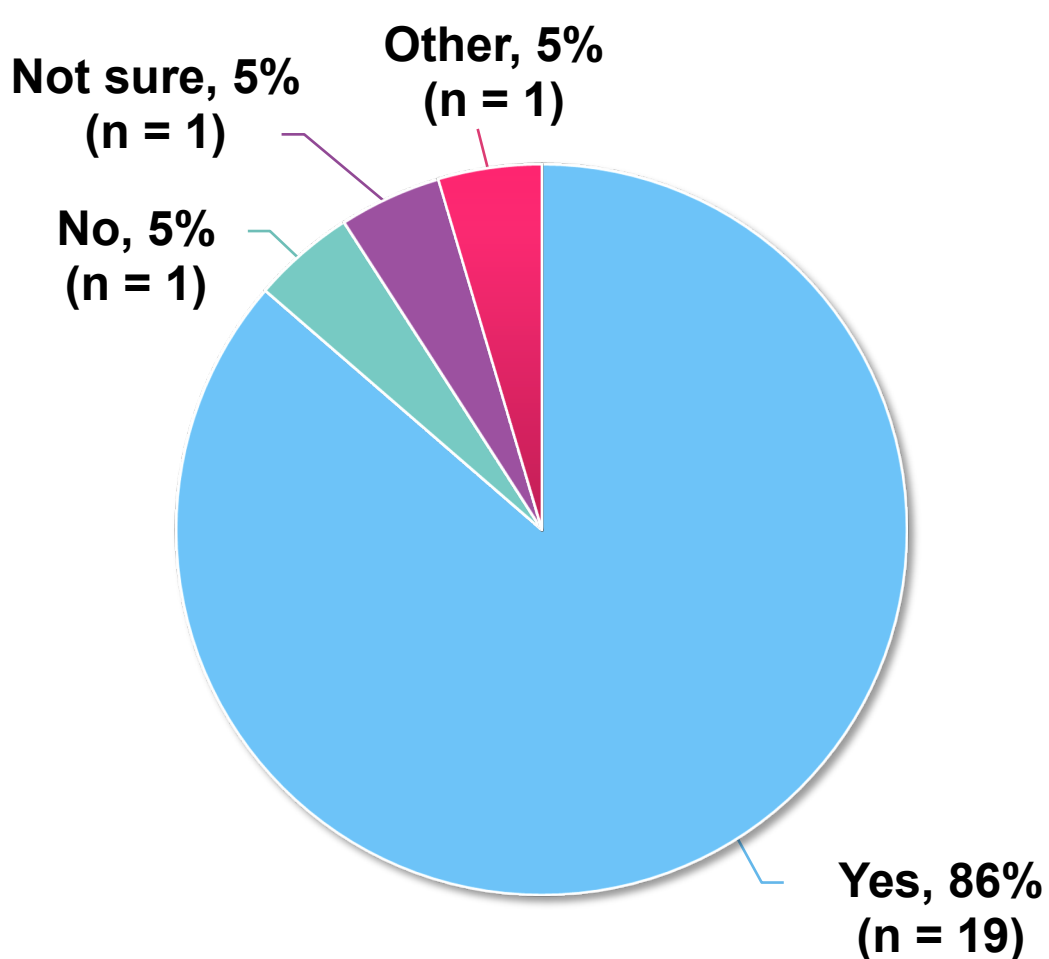
	US trofinetide prescribers (N = 697) ^a	US trofinetide prescriptions (N = 1553) ^a
Non-COE providers, n (%)	665 (95.4)	962 (61.9)
COE providers, n (%)	32 (4.6) ^b	591 (38.1)

^aAs of May 2024. ^bOne eligible prescriber was associated with zero prescriptions
COE, center of excellence

Trofinetide Dose Titration Impact on Tolerability

- In total, 86% (n = 19) of survey respondents indicated that titrating trofinetide improves tolerability in treatment-naïve patients (**Figure 1**)
- Specific tolerability improvements observed by respondents included decreased diarrhea severity (77%, n = 17), decreased trofinetide discontinuations (73%, n = 16), improved caregiver quality of life (64%, n = 14), and improved patient quality of life (59%, n = 13) (**Figure 2**)

Figure 1. Survey Respondents' Assessment of Impact of Trofinetide Dose Titration on Tolerability



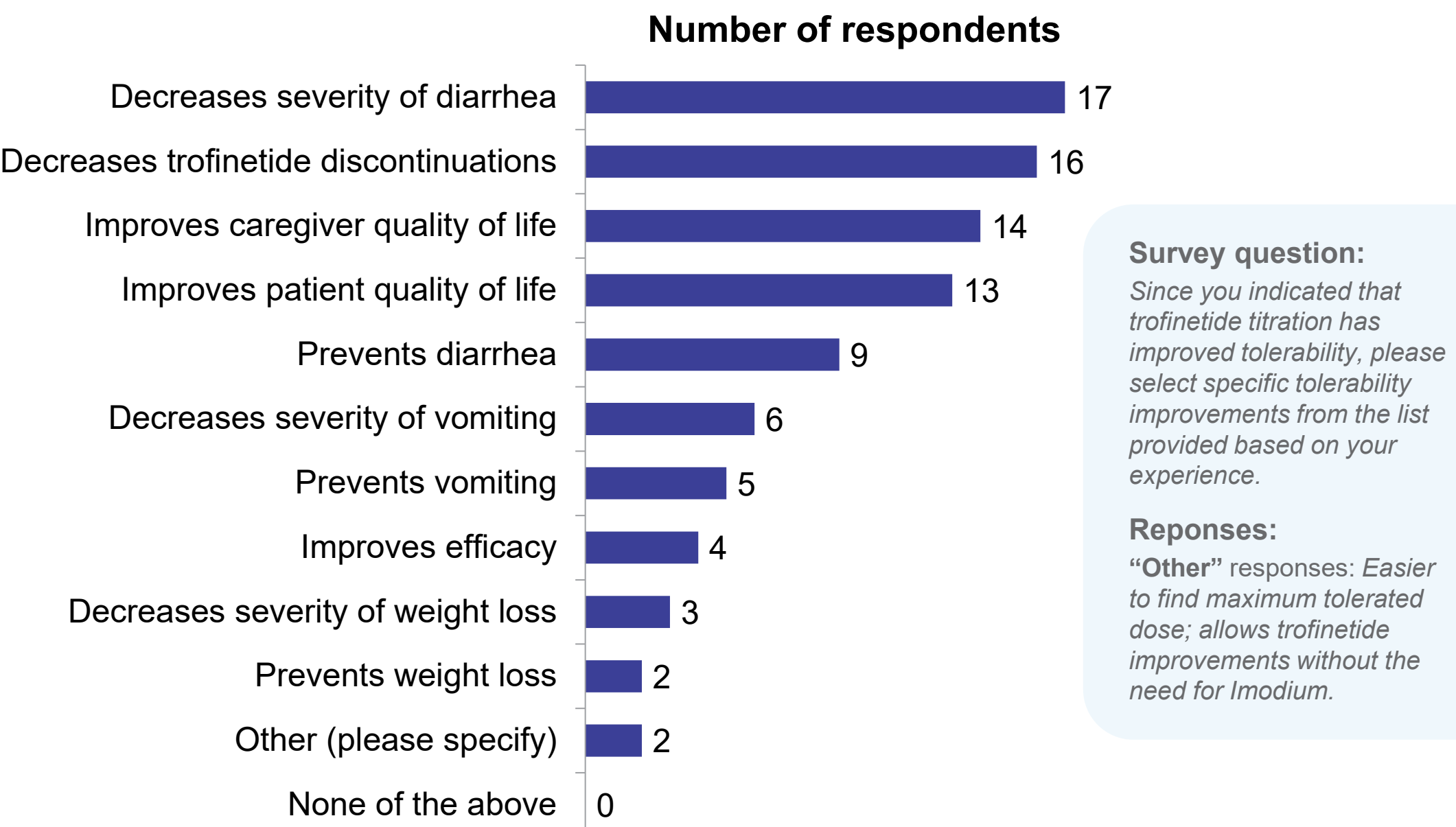
Survey question:

As compared with your experience when starting trofinetide at labeled dose (ie, clinical trial setting or real-world setting), has titration helped improve overall tolerability of trofinetide? If no or not sure, please explain how in comment field below.

Responses:

"No": Some patients do not like the taste; another vomits even with 5 mL dose.
"Not sure": I think there are patients that it doesn't matter for, patients it is critical for, and patients that don't tolerate no matter what we do.
"Other": Did not participate in the trofinetide clinical trials and/or I have never started patients at the full weight-banded dose.

Figure 2. Trofinetide Tolerability Improvements With Dose Titration Reported by Survey Respondents



Survey question:

Since you indicated that trofinetide titration has improved tolerability, please select specific tolerability improvements from the list provided based on your experience.

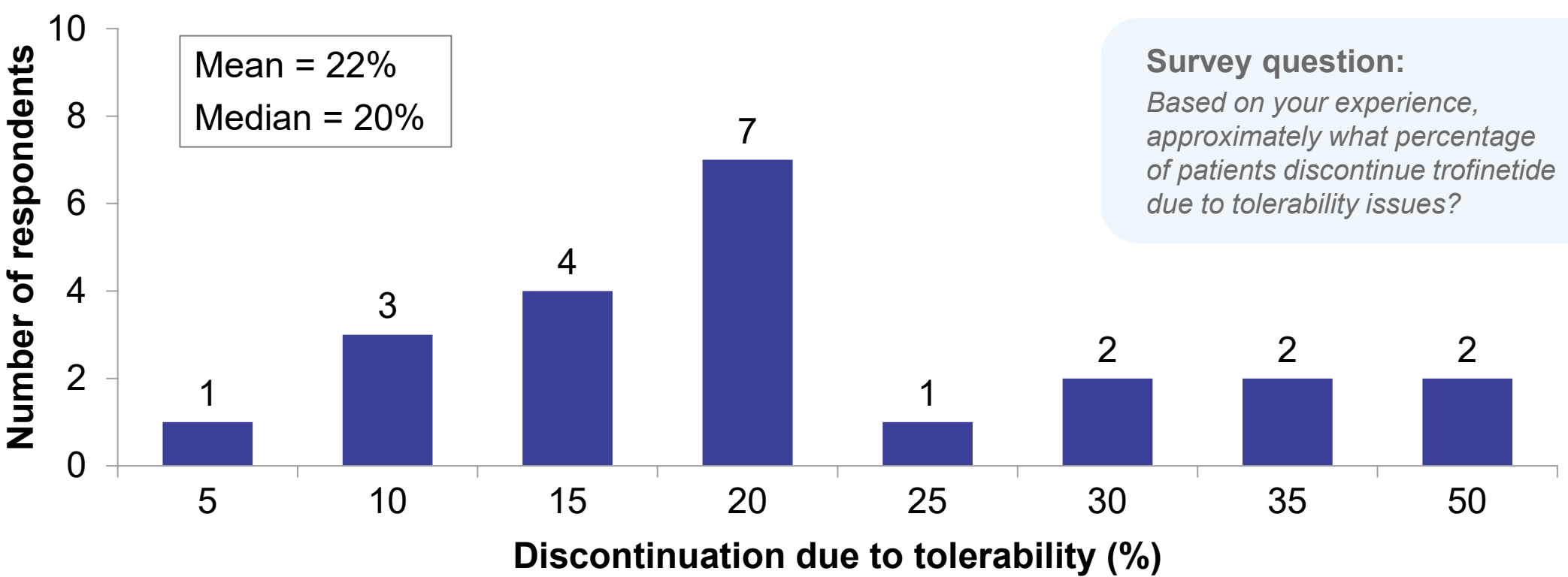
Responses:

"Other" responses: Easier to find maximum tolerated dose; allows trofinetide improvements without the need for Imodium.

Trofinetide Tolerability-Related Discontinuation

- Survey respondents indicated that approximately 20% of patients may still discontinue trofinetide due to tolerability issues (**Figure 3**)
- Trofinetide discontinuation due to lack of efficacy was estimated to be much lower at approximately 5–8% (**Figure 4**)

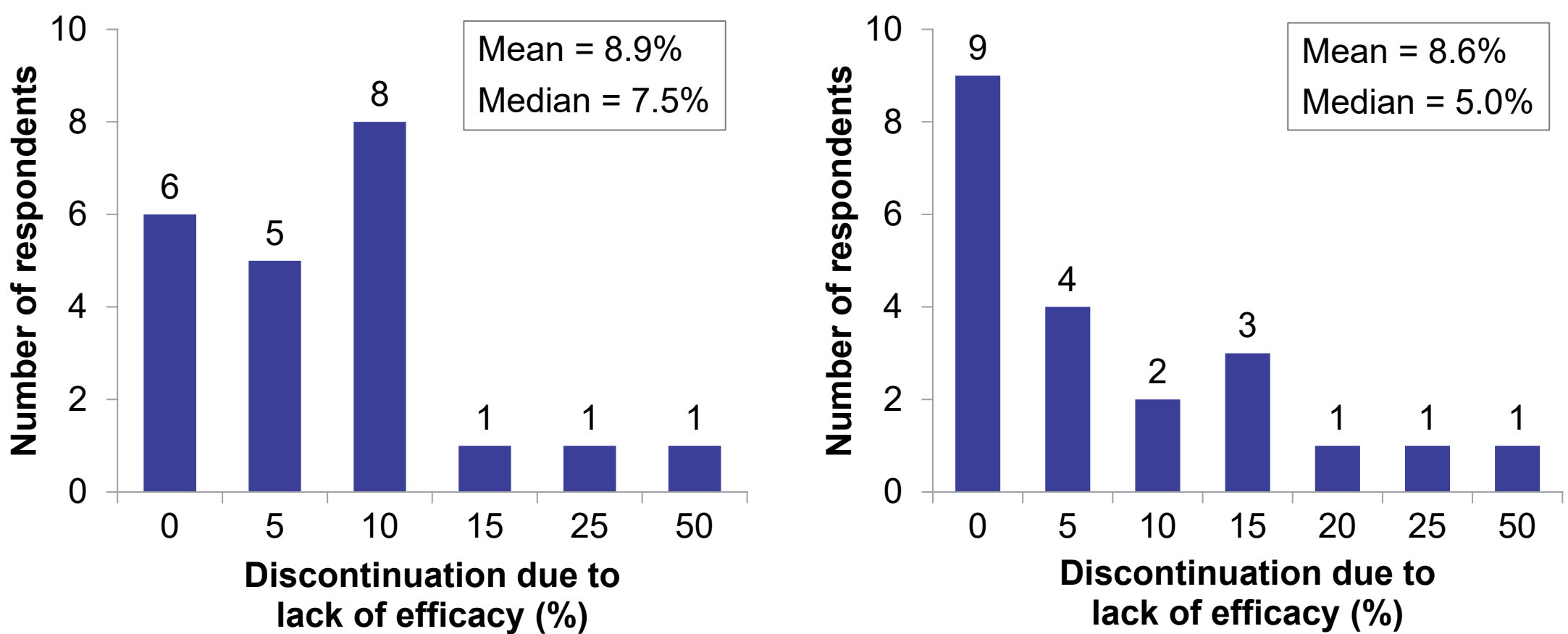
Figure 3. Trofinetide Discontinuation Due to Tolerability Issues



Survey question:

Based on your experience, approximately what percentage of patients discontinue trofinetide due to tolerability issues?

Figure 4. Trofinetide Discontinuation Due to Lack of Efficacy: (A) Discontinuation Due to Lack of Efficacy in Patients Who Achieve Full Weight-Banded Dose; (B) Discontinuation Due to Lack of Efficacy in Patients on Sub Weight-Banded Doses



Survey questions:

Have you or do you currently have any patients on a full weight-banded dose? If yes, based on your experience, approximately what percentage of patients on full weight-banded dose discontinue due to lack of efficacy? Have you or do you currently have any patients on a sub weight-banded dose? If yes, based on your experience, approximately what percentage of patients on sub weight-banded dose discontinue due to lack of efficacy?

CONCLUSIONS

- Prescribers believe trofinetide titration helps with overall tolerability, specifically to decrease diarrhea severity and treatment discontinuations while improving patient and caregiver quality of life
- Tolerability issues may persist in some patients, which can lead to discontinuation
- Prescribers believe discontinuation due to lack of efficacy remains low

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DISCLOSURES

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